ON THE ESSENTIAL OIL OF TAIWANIA CEDAR.

By Kinzo KAFUKU and Ryo KATO.

Received January 9, 1931. Published March 28, 1931.

The Taiwania cedar is one of the five big conifers indigenous to Formosa and is found along the central mountain range at an altitude of 6,000 to 7,000 ft. above sea level. It closely resembles Japanese Cryptomeria cedar (*Cryptomeria japonica*, D. Don.) in appearance, hence its Latin name,—*Taiwania Cryptomerioides*, Hayata. Its essential oil has hitherto never been studied but as it has a peculiar pleasant smell of its own, the authors undertook to investigate the nature of its volatile constituents, if any.

The material for examination forwarded by the Government Forestry Department at Taiheizan (Mt. Taihei) represented several root-stumps of a big, freshly hewn tree, of about 100 years of age, and they were chopped into small pieces of $1 \times 3 \times 8$ cm. in size, and put into a still. On prolonged steam distillation the authors obtained a very viscous oil of faintly yellow tinge with characteristic pleasant aroma, the yield amounting to 0.23% by weight of the material used. The oil, though very viscid, showed no tendency to deposit solid crystalline substance even on cooling with freezing mixtures. On fractional distillation it gave no terpene or terpene alcohol fractions, but seemed to consist practically of sesquiterpenes and sesquiterpene alcohols,—viz. about 34% cadinene, 2–3% humulene and caryophyllene, and 46% sesquiterpene alcohol. This last mentioned sesquiterpene alcohol closely resembled that isolated by L. Ruzicka[1] from West Indian sandalwood oil, in such respects as, the boiling point, the formation of hydrochloride, unaction towards phthallic anhydride, etc. etc. Thus, it is of interest whether this oil can be used or not as a substitute for the aforesaid oil for therapeutic purposes as a drug.

Experimental.

The oil directly after steam distillation, on being dried over anhydrous sodium sulphate, showed the following constants:—

d_4^{15}	0.9593
n_D^{15}	1.5104
α_D^{15}	−2.00°

(1) *Rec. trav. chim. Pay-Bas*, **47** (1928), 370, 381.

Acid value	0.38
Ester value	10.52
Do. after acetylation	83.00
Specific viscosity	137.1
Turbidity number (alcohol)	7.5(1)

On shaking the oil with 40% sodium bisulphite solution, no formation of crystalline precipitate was observed, from this it follows likely that the oil contained neither aldehyde nor ketone. The result of five consecutive fractional distillations with Widmer's dephlegmator, is shown below. (Diagrammatically in Fig. 1.)

Fraction	Boiling point	Pressure	Distillate %
(1)	113°—115°	10 mm.	0.28
(2)	115°—120°	do.	0.16
(3)	120°—125°	do.	1.13
(4)	125°—130°	do.	2.06
(5)	130°—133°	do.	21.00
(6)	133°—135°	do.	13.70
(7)	135°—140°	do.	0.49
(8)	140°—145°	do.	1.23
(9)	145°—150°	6 mm.	46.20

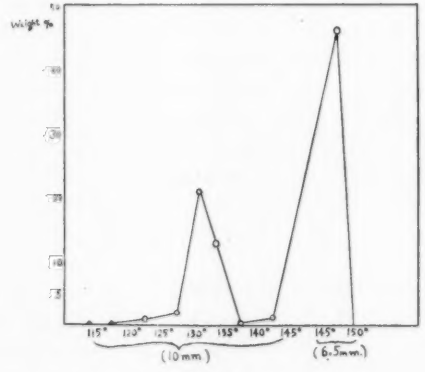


Fig. 1.

(1) Number of c.c. of water required to produce a permanent turbidity to 10 c.c. of an absolute alcohol solution of the oil in question (2 c.c. in 10 c.c. of alcohol).

The properties of these fractions are as follows:—

Fraction	d_4^{15}	n_D^{15}	α_D^{15}	M. R.
(1)	0.9104	1.4913	− 5.40°	—
(2)	0.9097	1.4979	− 1.40°	—
(3)	0.9089	1.5002	+ 1.08°	66.04 as $C_{15}H_{24}$
(4)	0.9134	1.5050	+ 7.20°	66.24
(5)	0.9189	1.5090	+35.20°	66.30
(6)	0.9215	1.5110	+54.60°	66.36
(7)	0.9641	1.5110	−17.40°	—
(8)	0.9715	1.5104	−33.40°	—
(9)	0.9742	1.5093	−40.46°	68.01 as $C_{15}H_{26}O$

It is noteworthy that in the foregoing table, the first two fractions and the last three are laevo-rotatory, while the rest are all dextro-rotatory, and that the fraction (5) which forms the greater part of the sesquiterpene fraction still contains oxygen to an extent of 2.6%, while the next (6) is practically pure hydrocarbon. From these, it follows that there may be a certain oxygenous compound of laevo-rotatory nature in the lower boiling portions. Whether this oxygenous compound be of terpenic alcoholic nature or not, we leave it for the future to decide.

The Sesquiterpenes. From considerations on the boiling behaviour and other physical constants, it seemed most probable that the fractions (3), (4), (5), and (6) consisted for the most part of dicyclic sesquiterpenes, so that the authors tested for the presence of caryophyllene and humulene with the fractions (3) and (4), and of cadinene with (5) and (6).

Thus, 0.5 gr. each of (3) and (4), was dissolved in an equal volume of absolute ether, and a dry current of nitrosyl chloride was passed in the cold as suggested by Ehestädt, and stood overnight in the ice chamber, then ether expelled and treated with methyl alcohol, when, an amount of crystalline substance separated out. Then it was fractionally recrystallized from methyl alcoholic solution and the resulting nitrosochloride tested for the melting point.

It was found that the nitrosochloride from (3) melted at 165°–166°, while that from (4) at 105°–106°. That the former was identical with humulene nitrosochloride, could be proved by the unlowering of its melting point on admixture with humulene nitrosochloride from oil of *chamaecyparis Obtusa*, Sieb. et Zucc., but the latter, on examination, seemed likely to be a mixture of cadinene nitrosochloride with some other higher-melting nitrosochloride.

Thus, they were once more fractionated under 10 mm. pressure, and it was possible to separate them into a lower boiling inactive, and a higher boiling active fractions. These afforded on treatment with nitrosyl chloride following Ehestädt's method,[1] two nitrosochlorides, the one melting at 165°–166°, and the other at 175°. The former was of course identical with humulene nitrosochloride, and the latter proved to be that of caryophyllene, which identity was affirmed by observing the mixed melting point with a known sample of caryophyllene nitrosochloride from Chamaecyparis oil. This latter nitrosochloride with m.p. 175°, showed an optical activity of +3.82° (0.423 gr. in 10 c.c. of chloroform).

Nextly an attempt was made to prepare nitrosites but it was altogether fruitless, and no crystalline substance could be obtained. But the action of cold glacial acetic acid solution of nitric acid on a mixture of 2 c.c. each of the sesquiterpene, isoamyl nitrite, and glacial acetic acid, afforded crystalline nitrosates from both, which after recrystallization from methyl alcohol, melted both at 162° and was proved to be humulene nitrosate (mischproben).

The fraction (5) was boiled over metallic sodium for six hours to get rid of oxygenous substances, and then rectified in vacuo, and in this way, a rather pure product with the following constants was obtained.

B.p.	130°—131.5° / 10 mm.
d_4^{20}	0.9183
n_D^{20}	1.5093
α_D^{20}	+34.62°
M.R.	66.36; 66.15 calc. as $C_{15}H_{24}$ $\overline{=}_2$.

On Liebermann's colour test, the hydrocarbon produced indigo blue colour which gradually turned into blue and then pink. If dissolved in chloroform and a drop of concentrated sulphuric acid added, it imparted to the solution a deep red coloration. This agrees with the behaviours of cadinene, so that tests in this direction were carried out. One gram of the sample was dissolved in an equal amount of absolute ether, and a current of dry hydrogen chloride gas was passed into the ice-cold solution, after twenty minutes an amount of crystals separated out which was kept overnight, then ether and hydrogen chloride driven off in vacuo, and the resulting semisolid mass was thoroughly washed with cold glacial acetic acid and then recrystallized from acetic ether. The white needle crystal thus obtained showed a melting point 117°—118°, whose identity with cadinene dihydrochloride could be proved by "mischproben" method.

(1) *Schimmels Report*, April **1910**, 164.

The nitrosate and the hydrobromide were prepared in the usual manner and after due purifications it was observed to melt at 110°—111° and 124°—125° respectively, which is in accordance with the data about the corresponding derivatives of cadinene. The fraction (6) had practically the same constants as this rectified product from (5) and on repeating the experiments as above, it gave precisely the same results. Only, it is worth mentioning, that in the second experiment, the hydrochloride (m. p. 117°—118°) offered an optical activity of −39.64° (in chloroform solution), and that the cadinene regenerated from this hydrochloride rotated a laevorotation of −47.42°, whereas the original sesquiterpene gave a rotatory power +56.60°. This is in accordance with the description by Semmler[1] that the hydrochloride obtained either from *d*- or *l*-cadinene, as well as the revived cadinene from the hydrochloride are all laevo-rotatory.

The oxidation of cadinene has been studied by L. Ruzicka and M. Stoll,[2] and by D. T. Gibson, J. M. Robertson, and J. Sword,[3] but no crystalline compound other than cadinene glycol has been obtained. The authors oxidized cadinene with acetone permanganate and obtained a substance melting at 142°—143° with a composition corresponding to the formula $C_{12}H_{22}O_2$. It was carried out in the following manner. To a mixture of 20 gr. of the rectified hydrocarbon from (6), 150 gr. of acetone, and 40 gr. of water under stirring, 20 gr. of finely powdered potassium permanganate was added in small portions and the temperature maintained at 30°—40° during the reaction. After the reaction was over, the mass was subjected to steam distillation to drive off acetone and unacted hydrocarbon, then the residue was extracted with ether. The ether extract was evaporated and distilled in vacuo, when, 12 gr. of unacted cadinene came over, and then about 4 gr. of higher-boiling oxidation product distilled at about 140° under 4 mm. pressure. This product was treated with petroleum ether when a crystalline substance deposited which melted at 142°—143° after purification. The substance, on analysis, showed the composition $C_{12}H_{22}O_2$.

Anal. Subst.=0.1088, 0.1103; CO_2=0.2895, 0.2930; H_2O=0.1070, 0.1100 gr. Found: C=72.56, 72.44; H=10.87, 11.08%. Calc. for $C_{12}H_{22}O_2$: C=72.70; H=11.10%.

As for the exact character of this substance the authors wish to communicate on the next available occasion, and retain it for the present.

The Sesquiterpene Alcohol. The fraction (9) practically consisted of sesquiterpene alcohol, as its physical properties as well as the analytical data show :—

(1) "Die ätherischen Oele," Bd. 2, S. 553.
(2) *Helv. Chim. Act.*, **7** (1924), 84.
(3) *J. Chem. Soc.*, **1926**, 164.

B.p.	145°—150°/6.5 mm.
d_4^{15}	0.9742
n_D^{15}	1.5093
α_D^{15}	−40.46°
M.R.	68.01; calculated as $C_{15}H_{26}O$ $\overline{\overline{=}}$ =68.12.

Anal. Subst.=0.1267; CO_2=0.3882; H_2O=0.1293 gr. Found: C=81.42; H=11.34%. Calc for $C_{15}H_{26}O$: C=81.11; H=11.74%.

This fraction, on Liebermann's test, gave indigo blue colour at first which faded into pink, while the chloroformic solution, on addition of a few drops of concentrated sulphuric acid, turned into dark blue and changed into red in course of time.

Fifty grams of the fraction was boiled over a calculated amount of metallic sodium for 15 hours, the unacted oil was driven off in vacuo, the residual viscous mass of the alcoholate was decomposed by alcoholic sulphuric acid, then an excess of water was added and it was extracted with ether. The ethereal solution was washed out with water, dried, evaporated, and then distilled under a pressure of 6 mm. mercury. The distillate showed the following constants:—

B.p.	141°—143°/6 mm.
d_4^{20}	0.9692
n_D^{20}	1.5045
α_D^{20}	−42.56°
M.R.	67.88; calculated as $C_{15}H_{26}O$ $\overline{\overline{=}}$ =68.01.

Anal. Subst.=0.1355; CO_2=0.4032; H_2O=0.1439 gr. Found: C=81.15; H=11.79% Calc.: C=81.11; H=11.70%.

Three grams of this substance, dissolved in dry ether was treated with a current of dry hydrogen chloride, when, a quantity of crystalline compound precipitated. Ether and excess of hydrogen chloride was then driven off at room temperatures, and the crystalline substance remaining behind was well washed with cold glacial acetic acid, drained until dry on the porous porcelain plate and then recrystallized from acetic ether. The pure hydrochloride showed a melting point 117°—118°, and proved to be identical with cadinene dihydrochloride as no lowering of melting point occurred on mixing it with cadinene dihydrochloride from other sources. Exactly the same thing had been experienced by Semmler and Jonas[1] in handling the sesquiterpene alcohol from galbanum oil, and they had given the name "cadinol" to it. They had stated that it represented a tertiary sesqui-

(1) *Ber.*, **47** (1914), 2068.

terpene alcohol, and that it was liable to break into cadinene and water, but failed to prepare any definite crystalline derivatives therefrom. For the sake of comparison, their data as regards this sesquiterpene alcohol, and the authors' data are given below :—

	Semmler and Jonas	Kafuku and Kato
B.p.	155°—165° / 15 mm.	141°—143° / 6 mm.
d^{20}	0.9720	0.9692 ($_{30}$°)
n_D^{20}	1.50702	1.5045 ($_{30}$°)
α_D^{20}	+22°	−42.56° ($_{30}$°)
M.R.	67.97	67.88

With a view to obtain a crystalline phenyl urethane, the purified alcohol was let react with phenyl isocyanate. For this purpose, 2.2 gr. of the freshly distilled substance and 1.2 gr. of phenyl isocyanate was mixed in the warm and kept for 20 days in a desiccator, when the mixture congealed into a crystalline mass. Then, it was treated with petroleum ether and got rid of diphenyl urea in the usual manner, and at last, a crude phenyl urethane m.p.=128°–130° was obtained, which after recrystallizations from alcohol showed a melting point 134°–135°.

The attempt to prepare the benzoate, the acid phthalate, the paranitrobenzoate, the bromide, or the xanthogenate, turned out altogether to be futile, and no crystalline compound was obtained. Only, it is worthy of note that the petroleum ether solution of the sesquiterpene alcohol, on treatment with an aqueous chromic acid solution assumed a characteristic red colouration, which according to Wienhaus[1] showed the formation of chromic acid ester. Even though it was impossible to get any crystalline chromic ester, this colouration and its poor affinity towards phthalic anhydride suggests that the authors' sesquiterpene alcohol also to be of a tertiary nature.

Ten grams of the rectified product from (9) was oxidized in aqueous acetone solution with 25 gr. of potassium permanganate at 50°–60°, the resulting mass was steam distilled to expel the unoxidized oil, and then, the aqueous residue, as well as the manganic mud, were separately extracted with ether, the ethereal solutions united and evaporated, when a small quantity of a yellowish oil together with a little crystalline residue remained behind. On standing for a length of time, the whole coalesced into a gruel-like mass, which was dried on the clay plate and the crystalline body recrystallized from benzol. The resulting crystal melted at 170°, but, on account of the small quantity available, nothing has been done to determine the nature of the substance.

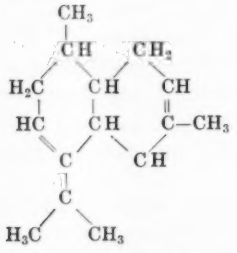
(1) *Ber.*, **47** (1914), 329.

Thirty grams of the substance was dissolved in an equal amount of pure formic acid, and warmed on the water bath for fifteen minutes, then the acid was neutralized with caustic soda, the hydrocarbon thus formed was extracted with ether, ether evaporated off, and the hydrocarbon boiled over metallic sodium at 165°–180° for 4 hours, and then rectified in vacuo. The distillate had the following properties:—

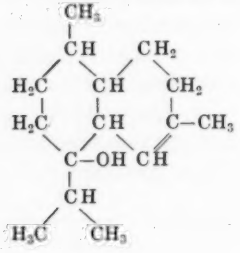
B.p.	124°—135°/10 mm.
d_4^{20}	0.9209
n_D^{20}	1.5100
α_D^{20}	−51.08°
M.R.	66.25 as $C_{15}H_{24}\overline{\overline{=}}_2$ =66.15

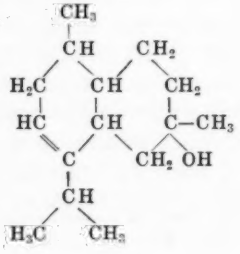
This hydrocarbon gave a dihydrochloride m.p. 117°–118°, and a dihydrobromide m.p. 124°–125°, which turned out to be identical with those of cadinene, (mischproben). Also a nitrosate melting at 110°–111° was obtained in the usual manner. From these it is obvious that the product of dehydration is cadinene.

From the foregoing experiments it seems possible that the authors' sesquiterpene alcohol might be identical with Semmler's cadinol, but considering the assumed constitutional formula for cadinene, there still remains much to be determined before the identity is claimed. Supposing the constitutional formula for cadinene to be

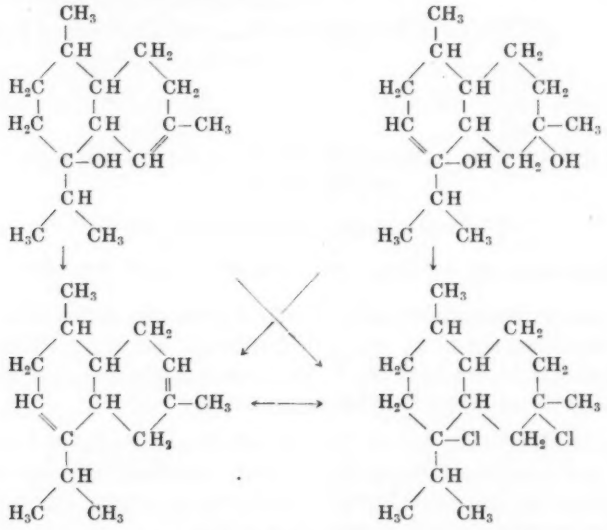


the following two sesquiterpene alcohols of the formulae





may both be responsible for the formation of cadinene dihydrochloride by the action of hydrogen chloride, and at the same time the dehydration to cadinene by formic acid, thus:—



It therefore remains for the authors to determine which of these two formulae should more reasonably be adopted for the sesquiterpene alcohol in question. The authors hope to discuss the subject by studying the oxidative disintegration of the alcohol on the next available opportunity. For the present, the authors wish to name their sesquiterpene alcohol as "taiwanol," as it originates from *Taiwania Cryptomerioides*, Hayata.

Summary.

1. The wooden chips of *Taiwania Cryptomerioides*, Hayata, gives on steam distillation 0.23% of an oil, consisting chiefly of sesquiterpene and sesquiterpene alcohol.

2. The sesquiterpenes in the oil are chiefly cadinene, with a little humulene and caryophyllene.

3. From the cadinene, a new oxidation product $C_{12}H_{22}O_2$ (m.p.=142°–143°) was obtained.

4. The sesquiterpene alcohol in the oil, to which the authors suggest the name "taiwanol," closely resembles cadinol of Semmler and Jonas. From cadinol no crystalline phenyl urethane could be obtained, but in case

of taiwanol, it affords a crystalline pheyl urethane melting at 134°–135°, and furthermore, it gives a neutral oxidation product (m.p. 170°) if oxidized with permanganate in acetone solution.

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UEBER DIE ADSORPTION BISUBSTITIERTEN BENZOLEN.

Von Bun-ichi TAMAMUSHI.

Eingegangen am 7. Februar 1931. Ausgegeben am 28. März 1931.

In folgenden Untersuchungen wurde zuerst die Adsorption einiger bisubstitierten Benzolen: *o*-, *m*-, *p*-Nitrophenol, *o*-, *m*-, *p*-Nitranilin, *o*-, *m*-, *p*-Dinitrobenzol, durch Kohle in benzoligen Lösungen gemessen, und dazu wird eine theoretische Bemerkung gemacht.

I. Man schüttelte die 100 c.c. Lösung mit 10 gr. Tierkohle (von Merck) zusammen und bestimmte deren Solutgehalt gravimetrisch vor und nach der Adsorption, indem man das Lösungsmittel in einem Platintiegel bei niedriger Temperatur sorgfältig verdampfen liess.

Die folgenden Tabellen 1–3 zeigen die Ergebnisse, wobei c die Konzentration in Millimol in Litre and a die adsorbierte Menge in Millimol je Gramm Kohle bedeuten. Die Versuchstemperatur ist dabei auch angezeigt.

Tabelle 1.

$t = 25°C.$

Substanz	c	a
o-Nitrophenol	130.660	0.345
	58.993	0.180
	43.876	0.151
m-Nitrophenol	90.653	0.323
	20.144	0.144
p-Nitrophenol	68.344	0.374
	35.970	0.251
	20.144	0.173

Tabelle 2.

$t = 25°C.$

Substanz	c	a
o-Nitranilin	52.894	0.065
	34.059	0.043
	6.909	0.011
m-Nitranilin	52.885	0.094
	18.840	0.058
p-Nitranilin	23.188	0.102
	18.840	0.087

Tabelle 3.

t=18-20°C.

Substanz	c	a
o-Dinitrobenzol	58.929	0.048
	25.000	0.030
	8.344	0.015
m-Dinitrobenzol	54.762	0.018
	36.309	0.014
	11.902	0.009
p-Dinitrobenzol	55.953	0.030
	23.512	0.018
	11.309	0.012

Weiter, wie Fig. 1-3 zeigen, gilt durchaus die Freundlichsche Adsorptionsisotherm

$$a = k C^{\frac{1}{n}},$$

worin $\frac{1}{n}$ gleich 0.53 fuer Nitrophenol, 0.57—0.93 fuer Nitranilin und 0.36—0.57 fuer Dinitrobenzol.

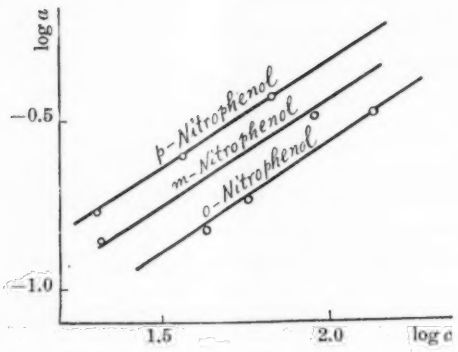
log a
−0.5
−1.0
p-Nitrophenol
m-Nitrophenol
o-Nitrophenol
1.5
2.0
log c

Fig. 1.

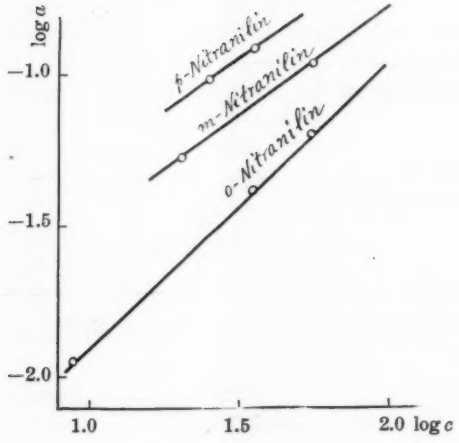
log a
−1.0
−1.5
−2.0
p-Nitranilin
m-Nitranilin
o-Nitranilin
1.0
1.5
2.0 log c

Fig. 2.

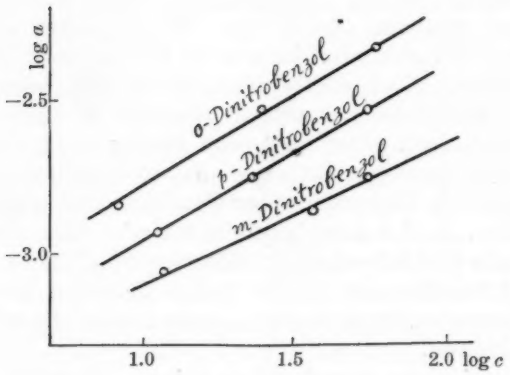

Fig. 3.

Die Adsorption vermindert sich in der Reihe $p > m > o$ bei Nitrophenol sowie bei Nitranilin, aber bei Dinitrobenzol in der Reihe $o > p > m$.

II. In Bezug auf diese experimentellen Ergebnisse, sei folgende Ueberlegung gestattet. Zunächst hat die Adsorption in Lösungen einen bekannten Zusammenhang mit der Löslichkeit, und es steht zu erwarten, dass die Substanz, welche schwerer löslich ist, stärker adsorbiert wird. Fuer den Fall von Nitrophenol sowie von Nitanilin gilt diese Regel qualitativ, da sich die Löslichkeit dieser Verbindungen in Benzol vergrössert in der Reihe $p < m < o$, während sich die Adsorption in dieser Reihe vermindert. Auch bei Dinitrobenzol, wurde *m*-Dinitrobenzol, das leichst löslich ist, am schwersten adsorbiert.

Unerwarteterweise wurde aber *o*-Dinitrobenzol, das beträchtlich leichter löslich ist als *p*-Dinitrobenzol, etwas stärker adsorbiert als *p*-Dinitrobenzol.

Diese letzte Regelwidrigkeit möchte ich provisorisch Dipoleffekt nennen, womit ich darauf hindeuten möchte, dass die Adsorptionskraft auch in Lösungen teilweise als elektrostatisch aufgefasst werden könnte, soweit wir die polaren Molekeln im Betracht nehmen.[1] Vermutlich werden also die Molekeln, die ein grosses Dipolmoment besitzen, durch Adsorbens stark angezogen, etwa aus dem analogen Grunde, weswegen bei solchen polaren Molekeln eine Molekülarassoziation erfolgt.

(1) Elektrostatische Theorien der Adsorptionskraft sind besonders bei Gas-fest Grenzfläche mit Erfolg aufgestellt worden. Verg. E. Hückel, "Adsorption u. Kapillarkondensation." (1928).

In den meisten Fällen, besonders wenn wir die Adsorption in wässerigen Lösungen studieren, wobei das Wasser selbst stark polar ist, würden die ganzen Verhältnisse kompliziert sein und kein Dipoleffekt wäre eindeutig bekannt. Doch dürfte dieser Effekt sich bemerkbar machen, wenn wir die Adsorption der polaren Molekeln in dipollosen benzoligen Lösungen untersuchen. Das natürliche Dipolmoment der Molekeln ist eigentlich auch in benzoligen Lösungen vielfach bestimmt worden.

Eine eingehende Diskussion ueber diese Frage soll hierbei nicht vorgenommen werden, da das experimentelle Material noch nicht genügt. In folgender Tabelle sind Schmelzpunkt, Löslichkeit (in Benzol), Molekularassoziation und Adsorption der bisubstitierten Benzolen zusammengestellt, damit wir einen charakteristischen Zusammenhang dieser Eigenschaften wahrnehmen können.

Der Pheil zeigt eine vergrössernde Reihe. Eindeutig ist der Zusammenhang fuer den Fall von Nitrophenol und Nitranilin. Wie es schon bekannt ist, sind Schmelzpunkt und Löslichkeit einander antiparallel,

Tabelle 4.

Substanz	S. P.(1)	D. M.(2) (10^{18})	M. A.(3)	L.(4) (gr.i. 100 c.c.)	A.(5)
o-Nitrophenol	45	3.10	1.02	70 ↑	
m-Nitrophenol	96	3.90	1.05	2.48	
p-Nitrophenol	113 ↓	5.05 ↓	1.09 ↓	1.33	↓
o-Nitranilin	72	4.45	1.04	14.23 ↑	
m-Nitranilin	112	4.72	1.08	2.15	
p-Nitranilin	118 ↓	7.1 ↓	1.25 ↓	0.53	↓
o-Dinitrobenzol	117 ↑	6.00 ↑	1.16 ↑	4.96	
m-Dinitrobenzol	91	3.7	1.04	34.37 ↑↓	↑↑
p-Dinitrobenzol	172 ↓	0.8	1.01	2.26	↓

(1) Schmelzpunkt. "Chemiker Kalender," 1931.

(2) Dipolmoment. Nitrophenol: J. W. Williams, *Fortschr. d. Chemie, Physik u. phys. Chemie*, Bd. 20, Ht. 5, 1930. Nitranilin und Dinitrobenzol: K. Höjendahl, *Phys. Z.*, **30** (1929), 391.

(3) Molekülarassoziation. Nitrophenol und Nitranilin, in etwa 50 Millimol benzoligen Lösungen: H. Shiba, Unveröffentlichte Arbeiten. Herr Shiba hat neulich die Molekülarassoziation zahlreicher polaren organischen Verbindungen ebullioskopisch untersucht. Dinitrobenzol: Nach meinen kryoskopischen Versuche in derselben Konzentration.

(4) Löslichkeit. Nitrophenol und Nitranilin: Nach meinen Versuche. Versuchstemperatur =25°. Dinitrobenzol: de Bryn, *Rec. Trav. Chim.*, **13** (1894), 116. Versuchstemperatur=18°.

(5) Adsorption. Verg. Tabelle 1–3.

während Dipolmoment bez. Molekülarassoziation mit dem Schmelzpunkt parallel stehen. Die Adsorption ist antiparallel mit Löslichkeit, somit parallel mit Dipolmoment.

Auch bei Dinitrobenzol sind Löslichkeit und Schmelzpunkt antiparallel einander, und zwar hat *m*-Verbindung ein Schmelzpunktsminimum bez. Löslichkeitsmaximum. Dipolmoment und Molekülarassoziation sind auch in diesem Falle einander parallel und vergrössern sich nach der Reihe $p < m < o$. Adsorption hat sein Minimum bei *m*-Verbindung, die am leichsten löslich ist, während fuer *o*- und *p*-Verbindung der Löslichkeitseinfluss von dem Dipoleffekt uebertroffen zu sein scheint.

Es sei an dieser Stelle Herrn Dr. H. Shiba mein Dank fuer seine freundliche Mitteilug ueber Molekülarassoziation ausgesprochen. Herrn Prof. M. Katayama bin ich fuer seine wertvollen Ratschläge zum wärmsten Dank verbunden.

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SINOMENINE AND DISINOMENINE. XXV. ON THREE DIFFERENT SINOMENINE-METHINES.

By **Kakuji GOTO** and **Hideo SHISHIDO.**

Received February 25, 1931. Published March 28, 1931.

In the previous note, published in 1926,[1] one of the authors (K.G.) reported preliminarily on the three different products of sinomenine [I], produced by the Hofmann decomposition. Now that the constitution of sinomenine is fairly well established,[2] we undertook the investigation again and could trace the relation of these three methines, the results of which will be published here with some necessary supplements and corrections to the former note.

When sinomenine iodomethylate was boiled with 2% NaOH (2 mol) for one minute, there is formed an iodine free substance, $C_{20}H_{25}NO_4$, of m.p. 179°. To this substance, formerly the name N-methyl-anhydro-sinomeninium-base and the constitution [II] had been given chiefly from the following three reasons.

(1) *Proc. Imp. Acad.*, **2** (1926), 167.
(2) In the XXIV report of this study, (*Ann.*, **485** (1931), 247), the results are partly summarized.

1. The extreme easy formation of this substance, compared with the other two methines.

2. The characteristic unstableness of this substance, which does not allow the recrystallization even from alcohol. This might indicate the splitting off of the double linking between $C_{(9)}$ and N.

3. Very weak halochromy with conc. H_2SO_4. All the methines of morphine and codeine are known to give strong colouration with this reagent.

Yet, the fact that the hydroiodide of this substance is totally different from the starting material was very singular, although this fact was not mentioned in that short note.

Now, we prepared the hydroiodide and iodomethylate of this substance carefully and found that these two salts give the same weak halochromy with conc. H_2SO_4. In addition to this, the fact that the iodomethylate of this substance is transformed into the iodomethylate of the secoud methine by cold 10% NaOH, which give an intense blue halochromy with H_2SO_4, reminded us of the transformation of α-methyl-morphi-methine into β-methyl-morphi-methine by alcoholic alkali. We are, therefore, inclined now to give this substance the methine constitution [III] and call it sinomenine-achro-methine.

As its iodomethylate, the sinomenine-achro-methine itself can be transformed into the methine, which gives an intense blue colour with conc. H_2SO_4. This methine was called α-sinomenine-methine in the previous note, but we wish to call it now sinomenine-violeo-methine, in order to avoid confusion with the prefixes of the six methyl-morphi-methines, since the relation of each sinomenine methine to the corresponding methyl-morphi-methine is not exactly determined. We believe, however, that the sinomenine-violeo-methine corresponds to the β-methyl-morphi-methine from the reasons, which will be given later.

From sinomenine iodomethylate, another methine, which gives a strong red halochromy against conc. H_2SO_4, is obtainable. At first, this methine was obtained by boiling sinomenine iodomethylate with 5% NaOH (5 mol) for a short time. In this treatment this methine is produced side by side with the violeo-methine, the yield of the both methines being extremely small (5—7%). Now, it was found that the crude sinomenine-achro-methine, recrystallized from alcohol and kept for years, transforms itself partly into this methine. That in this transformation, the sodium bicarbonate, which might be attached to the crude methine, may be the cause, was proved by the experiment that the iodomethylate of the achro-methine could be turned into that of this methine by boiling in methyl-

alcohol, added with a bit of sodium bicarbonate. This third methine was called β-sinomenine-methine in the previous note, but we propose now the new name sinomenine-roseo-methine for it. The iodomethylate of this roseo-methine was transformed, then, into that of violeo-methine by cold 10% NaOH.

The relation of these three sinomenine-methines is given in the Table 1 and their properties are summarized in the Table 2.

Table 1.

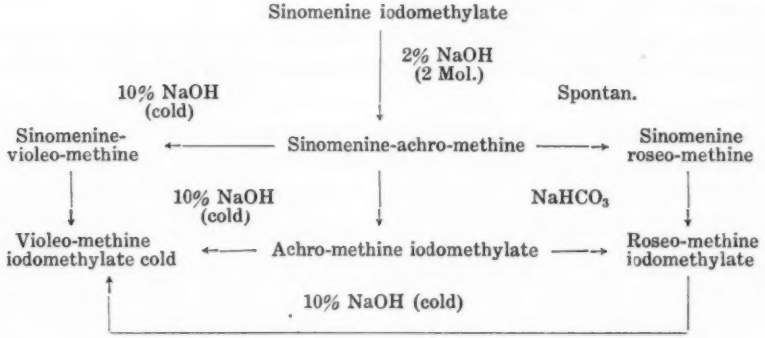


Table 2.

Substance Former names*	Sinomenine-achro-methine N-methyl-anhydro-sinomeniniumbase	Sinomenine-roseo-methine β-Sinomenine methine	Sinomenine-violeo-methine α-Sinomenine methine
M. p.	179°	163°**	172°—173°
Sol. in ether	easier soluble	difficultly sol.	almost not
$[\alpha]_D$	+72.58°	+135.70	+434.78°
Diazo-reaction	2,000,000th	100,000th	2,000,000th
Conc. H_2SO_4	faintly yellow	carmin red	deep blue
Fuming HCl	lyra	yellowish red	deep blue
M.p. of iodomethylate	212° (fr. water)	277° (fr. methanol)	209° (from water)
$[\alpha]_D$	−33.00°	−48.26°	+373.36°

The above three reactions are same with their corresponding free bases.

* *Proc. Imp. Acad.*, **2** (1926), 167.

** M.p. 263° in the above note is clearly a misprint.

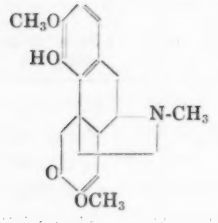
As regards the constitution of these three methines, we will now provisionally give the following explanation. In these three methines, no dislocation of the attaching groups and the linking point of dimethyl-aminoethyl group seems to have occurred. For, the achro-methine and the violeomethine (iodomethylate) could be very easily decomposed into sinomenol by the same methods as with the sinomenine itself. Though the roseo-methine has not been decomposed, the same argument could be applied to it, since its iodomethylate could be transformed into that of the violeo-methine. The cause of the difference in these three methines then may be due to the displacement of the double linkings, as Knorr and Robinson suspected to be the case in methyl-morphi-methines.

Now, we feel it is almost doubtless that the sinomenine-violeo-methine corresponds to the β-methyl-morphi-methine from the following considerations.

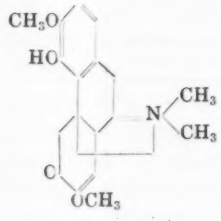
1) Its mode of formation (cold 10% NaOH).
2) Its high specific rotatory power.
3) Its intense blue halochromy with conc. H_2SO_4 and with fuming HCl.

R. Robinson,[1] based on the study of neopine, gave to the β-methyl-morphi-methine the constitution [VI]. This constitution seems to explain partly its high specific rotatory power as well as its intense halochromy. If this conception is not errornous, the sinomenine-violeo-methine may possess the constitution [V].[2]

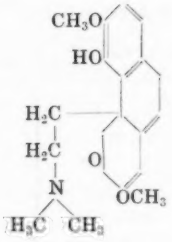
The question, which of the remaining two sinomenine-methines corresponds to the α-methyl-morphi-methine is difficult to say. But, from (1) its



I.



II.*

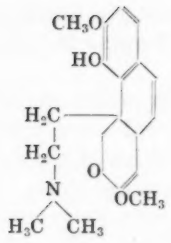


III.

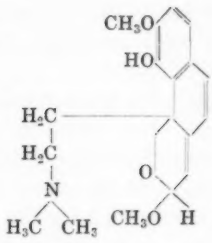
* Partly modified, with necessary corrections.

(1) R. Robinson, J. C. Smith, *J. Chem. Soc.*, **1926**, 903; compare also E. Speyer, Koulen, *Liebig's Annalen*, **438** (1924), 34, and R. S. Cahn, *J. Chem. Soc.*, **1926**, 2562.

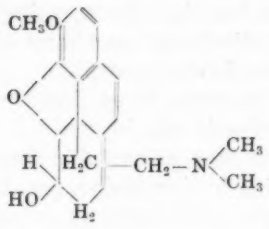
(2) An objection to this explanation may be the transposition of the double linking from α, β- to β, γ-position relating to the ketone group. But, after the text-book of Meyer-Jacobson (2. Edition, I, 1, p. 947), such a transposition is not without examples in unsaturated acids.



IV.



V.



VI.

very easy formation and (2) its very weak halochromy aganinst conc. H_2SO_4, we wish to give the constitution [III] to the sinomenine-achro-methine, taking the new double linking between C (9) and C (14). It is remarkable that all the derivatives of sinomenine, which have not the double linking in C (7) and C (8), stand stronger against the Hofmann decomposition. The iodomethylates of dihydro-sinomenine, of its demethoxy- and demethoxy-desoxo-derivatives are opend successfully in their C (9) and N-linking by boiling with 16.6% KOH over thirty minutes. This shows that the double linking in C (7) and C (8) makes easy the opening of the ring. If so, why should not the new double linking conjugate to the old one and enter between C (9) and C (14)? If we assume the double linking in C (9) and C (10) in the habitual way, the easy formation of the achro-methine could not be explained.

The position C (9) and C (14) is also convenient to explain the extremely weak halochromy of the substance. All the other methines of sinomenine series, which are produced by boiling 16.6% KOH or 25% NaOH over thirty minutes, give strong yellowish red or red halochromy against conc. H_2SO_4. This property is partaken by other hydrated phenanthrenes, which have a double linking in α, β-position to the not hydrated benzene nucleus, say, meta-thebainone[1] and benzylidene-*d*-thebenone.[2]

It may not be unreasonable to seek, therefore, the cause of the very weak halochromy of the achro-methine in the different position of the double linking from that of all the other methines.

As to the roseo-methine, we wish to give the constitution [IV] to it. The rearrangement of a β, γ-double linking to the benzene nucleus into the α, β-position by the action of alkali is well known in eugenol and allylbenzene. Whether this arrangement could be effected by a so mild reagent as $NaHCO_3$ is a question. Yet, seeing that the yield in this rearrangement

(1) C. Schöpf, H. Perrey, *Liebig's Annalen*, **483** (1930), 170.
(2) H. Wieland, M. Kotake, *Liebig's Annalen*, **444** (1925), 90.

is far less than the quantitative and that the roseo-methine gives an intense red halochromy as almost all the other methines, we propose this explanation for the present.

It seems to us that there must be some means, by which the above hypothesis can be verified or not. For example, the reductive method, which was so useful in determining the C (7)—C (8) position of the double linking in sinomenine, may be applied to the above three methines. Yet, all the preliminary experiments, carried out for the purpose, gave very unpromissing results, and we are forced to be satisfied with the above hypothetical explanations for the present. But the question whether the stage of sinomenine-achro-methine is passed or to be isolated in future in the methines, derived from morphine or condeine remains to be an interesting problem.

Experimental.

1. Sinomenin-achro-methine, [III]. Sinomenine iodomethylate (2 gr.) is boiled with 2% NaOH (20 c.c.; 2 mol) for one minute. The brownish coloured liquid is quickly cooled with water and saturated with CO_2 gas.

The reddish brown precipitate is then washed with hot water and dried on a porous plate. It is already crystalline. The raw yield amounts to 80% of the theoretical.

The purification is best effected through its sodium salt. When the crude product was poured on with ice-cold 10% NaOH, there is formed almost colourless phenolate of the substance. The latter is quickly collected on a glass-filter, washed with alkali and then redissolved in water. When the aqueous solution is again saturated with CO_2 gas, the achro-methine crystallises out in faintly brownish[1] flat prisms. One more recrystallization from much ether turns the substance into long prisms. They are still faintly coloured. This seems to be due to some impurity, which is quickly formed by the decomposition of the achro-methine itself. M.p. 179° (sintering at 173°). Its halochromy in conc. H_2SO_4 is very faintly yellow (almost colourless), so it is named sinomenine-achro-methine.

The properties of this methine is given in the first column of the Table 1.

Anal. Found: C=69.80, 70.10; H=7.05, 7.32; N=4.18; Methoxyl=18.15%.
$C_{20}H_{25}NO_4$=343 requires: C=69.97; H=7.28; N=4.08; Methoxyl=18.07%.
Sp. rotatory power, in chloroform: $[\alpha]_D^{16} = +(0.43 \div 0.1481) \times (25 \div 1) = +72.58°$.

(1) This brownish red substance seems to be produced by a partial decomposition of the achro-methine and gives a deep green halochromy with conc. H_2SO_4. The achro-methine seems to be turned into this substance at its melting point, but the substance itself could not be yet obtained in a crystalline form.

Hydro-iodide: long prisms, m.p. is very unsharp, but lies at 115~118° (sintering at 80°). Halochromy in conc. H_2SO_4 or in fuming HCl is the same with the free methine. (Found: I=27.18. $C_{20}H_{25}NO_4 \cdot HI$ requires I=26.96%) Hydro-chloride and hydrobromide is too hygroscopic for the analysis.

Iodomethylate: is prepared in methyl-alcohol without heating. It melts at 212° with decomposition. Halochromy is same as above.

Anal. Found: C=51.93, 51.98; H=5.76, 5.98; N=2.99; Methoxyl=12.48; I=26.09%. $C_{21}H_{28}NO_4I$=484.9 requires: C=51.96; H=5.77; N=2.89; Methoxyl=12.78; I=26.17%.

Sp. rotatory power, measured in water: $[\alpha]_D^{17}=(-0.11\div0.3333)\times(50\div0.5)=-33.00°$

Oxime: prepared in the ordinary way at room temperature. Recrystallisable from methylalcohol and ether into prisms collected in rosettes. Decomposes at 204~205° (losing water at 120°). (Found: N=7.79%. Calc. for the monoxime: N=7.82%).

Decomposition of the achro-methine with 66% KOH resp. with benzoyl-anhydride gave the same sinomenol resp. dibenzoyl-sinomenol as with sinomenine itself, the yield also being almost equal with the latter. The amine, evolved in the potash fusion, was also dimethyl-ethyl-amine. (The auri-chloride decomposed at 220° and the platini-chloride decomposed at 239°).

2. **Sinomenine-roseo-methine.** [IV]. The free base of this substance is formed, when the sinomenine iodo-methylate is decomposed with 5% NaOH (5 mol). But from the crude achro-methine, recrystallized from alcohol and kept for years, it was accidentally isolated in ca. 10% yield. The change might have been effected through the sodium bicarbonate, attached to the crystalls. This point was made clear with their iodomethylates. (See later on).

It is yellowish, melts at 163° and gives an intense red (carmin) halochromy in conc. H_2SO_4 and an yellowish red in fuming HCl. It is, therefore, called sinomenine-roseo-methine.

For the properties, see the second column of the Table 1.

Anal. Found: C=69.78; H=7.16; N=4.10; CH_3O-=18.24%. $C_{20}H_{25}NO_4$=343 requires: C=69.97; H=7.28; N=4.08; CH_3O-=18.07%.

Sp. rotatory power, measured in chloroform:

$$[\alpha]_D^{16}=(+1.03\div0.0759)\times(10\div1)=+135.70°$$

Iodomethylate. It was first noticed that the iodomethylate of the crude achro-methine, when prepared by boiling in methyl-alcohol, contains sometimes the iodomethylate of the roseo-methine. Therefore, in order to

transform the iodomethylate of the achro-methine into that of the roseo-methine, the former was boiled in ten times its weight of methyl alcohol with a bit of sodium bicarbonate for one hour and was set aside, after being filtered from the bicarbonate. On the next day, the crystalls deposited on the bottom was collected and recrystallized from methyl alcohol. It forms yellow long prisms, which melt and decompose at 276°. Admixture with the iodomethylate obtained in 1926, did not lower the melting point. Halochromy is the same with the free roseo-methine.

Anal. Found: C=52.05; H=5.88; N=2.84; CH_3O=12.42; I=26.05%.
$C_{21}H_{28}NO_4I$=484.9 requires: C=51.96; H=5.77; N=2.89; CH_3O=12.78; I=26.17%

Sp. rotatory power, measured in water: $[\alpha]_D^{17}=(-0.25\div0.1295)\times(25\div1)=-48.26°$

To prove the point, that the sodium bicarbonate effect this change, the pure achro-methine iodo-methylate was boiled in methyl alcohol without the addition of $HNaCO_3$. It was found that the iodomethylate, chrystallized out from the solution gave only the faintly yellow halochromy and melted also at 212°.

The yield of the roseo-methine was not good and the decomposition trial was not carried out with it. But the fact that it stands between the achro- and violeo-methines was proved by turning its iodomethylates into that of the violeo-methine by the action of cold 10% NaOH.

The only anormality of this methine is in the very diminished diazo-reaction, compared with the other sinomenine derivatives with the free C(1). We hope to clear away this question by a further study in a near future.

3. Sinomenine-violeo-methine. [V]. It was noticed, at the beginning of the study of sinomenine, that the action of boiling caustic alkali turns sinomenine into the substance which gives an intense bluish halochromy with conc. H_2SO_4. The substance, which is the cause of this colour, as well as its iodomethylate were isolated six years ago. This time, it was obtained from the achromethine and the relation was clearly settled.

When the achro-methine (1 gr.) is kept overnight in 10% NaOH (8 c.c.) and methyl-alcohol (4 c.c.) and then saturated with CO_2 gas, a precipitate is formed in the ice-cooled solution. This is collected and crystallized from chloroform by the addition of much ether. Yield about 20%, but, as will be described later, the change is almost the theoretical with the iodomethylate. It forms flat prisms and melts at 172~173°. It gives an intense blue halochromy with conc. H_2SO_4 as well as with fuming HCl. Hence the name sinomenine-violeo-methine is given.

The properties of this substance is given in the third column of the Table 1.

Anal. Found: C=70.03, 69.32; H=7.25, 7.20; N=4.23; CH_3O—=18.19%.
$C_{20}H_{25}NO_4$=343 requires C=69.97; H=7.28; N=4.08; CH_3O—=18.07%
Sp. rotatory power, measured in chloroform:

$$[\alpha]_D^{17}=(+0.19\div 0.2185)\times(250\div 0.5)=+434.78^\circ$$

The iodomethylate is formed from that of the achro-methine in an almost theoretical yield by the action of the cold 10% NaOH (5 times). The change seems to be complete in a few hours, judged from the halochromy, but the mixture is better to be left stand overnight for the precaution. It is well cooled with ice and saturated with CO_2 gas. As this substance is most difficultly soluble in water of the three, it crystallises out almost completely. It is colourless prisms collected in a form of a fun. M.p. 209° (dec., from water). Halochromy is the same as the free methine.

Anal. Found: C=51.84, 51.85, 51.60; H=6.01, 6.11, 6.20; N=2.99; CH_3O=12.64; I=26.29%. $C_{21}H_{28}NO_4I$=484.9 requires: C=51.96; H=5.77; N=2.89; CH_3O=12.78; I=26.17%.

Sp. rotatory power, measured in water: $[\alpha]_D^{17}=(+0.30\div 0.1607)\times(100\div 0.5)=+373.36^\circ$

The violeo-methine iodomethylate is already decomposed into sinomenol by boiling 3.3% NaOH for an hour (m.p. 172°). The use of 20% NaOH in this decomposition turns the greater part of sinomenol into disinomenol. This easy splitting off of the side chain is undoubtedly due to the strong tendency to aromatize of the nuclei II and III of the hydrated phenanthrene, since it contains a ketone group, which can enolize in presence of alkali. This is the reason why we must effect the transformation of the achro-methine into the violeo-methine in the cold.

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